UC contributes biotech breakthroughs

Researchers at UC are pioneering basic science and recombinant DNA technology in an array of agricultural and environmental sciences.

One recent advance that promises to improve human health has been UC Berkeley microbial biologist Bob Buchanan's exploitation of thioredoxin, a naturally occurring product, to make proteins such as those found in wheat and milk more easily digestible and less allergenic. Thioredoxin not only alleviates symptoms for allergy sufferers, but may also help people with celiac disease, a disorder that causes the intestines to react abnormally to the gluten in wheat, rye, barley and oats.

**Genetic engineering for disease resistance.** Other UC scientists have genetically engineered plants to resist disease. For example, biotechnology specialist Peggy Lemaux's lab at UC Berkeley was the first to successfully genetically engineer barley, introducing viral genes to make it resistant to barley yellow dwarf virus.

UC Berkeley plant pathologist and microbial ecologist Steve Lindow developed the widely publicized "ice minus" bacteria that can be used to prevent frost and disease damage on crops. Based on his earlier genetic engineering studies, Lindow has developed naturally occurring bacterial strain *Pseudomonas fluorescens* strain A506, commercially registered as Blightban A506 for use in California. It is most commonly used for fire blight and frost control in pears and apples.

A different gene-based approach to protecting crops is the focus of Brian Staskawicz's research. The UC Berkeley plant biologist and his lab team were the first to isolate a bacterial gene that triggers a defensive response in plants. This work has played a key role in discoveries of disease-resistance genes in plants. Also at UC Berkeley, plant geneticist Barbara Baker became the first person to clone a gene with natural resistance to viruses.

**Genetic engineering for insect control.** A research group at UC Davis, led by nematologist Valerie Williamson, discovered a resistance gene that is effective against both nematode and aphid. Williamson isolated the root-knot nematode-resistance gene Mi from tomato. Working with entomologist Diane Ullman, the group found that this same gene also confers resistance against potato aphids.

UC Davis entomologist Bruce Hammock's lab is working to incorporate genes into baculoviruses that control a critical insect hormone. The gene for a key enzyme that degrades the hormone has been isolated and sequenced by Hammock's lab, which is working to develop its use for biological insect control.

Baculovirus genes also confer resistance in plants. UC Davis plant pathologist David Gilchrist determined that programmed cell death, called apoptosis, plays a key role in plant infection. Apoptosis, an important process in genetic regulation and biochemical response of animals to disease, seems to fulfill a similar role in plants. To see if blocking apoptosis with a transgene would prevent disease in plants, Gilchrist and his colleagues inserted an anti-
apoptotic gene ffrom baculovirus into transgenic
tomato plants and found that these plants were
resistant to several diseases. Gilchrist hopes the
merging of plant and animal research on
apoptosis will lead to new methods for disease
protection and enhanced food safety.

Meanwhile at UC Berkeley, plant biologist
Sarah Hake was the first to clone a plant
homeobox gene — pivotal genes that set up en-
tire developmental pathways. In flies, for ex-
ample, the incorrect expression of these genes
has been shown to result in the formation of an
eye on the thorax.

Postharvest applications for crops. USDA/
UC Berkeley Plant Gene Expression Center
plant biologist Sakis Theologis was the first
person to clone and characterize a critical gene in
ethylene biosynthesis, which led to the creation
of the Endless Summer tomato and the use of
the technology to retard spoilage in other fruits
and vegetables.

New techniques for remediating environ-
mental contamination. UC Riverside chemical
engineers Wilfred Chen and Ashok
Mulchandani recently engineered a bacterium
that degrades organophosphate pesticides. The
scientists designed a gene that directs the
manufacture of a hybrid protein combining the
enzyme organophosphorus hydrolase (OPH)
with other structures that anchor the OPH to
the outer surfaces of bacterial cells. They then
inserted the gene into a harmless strain of E.
coli bacteria. Tested in paraethion- and
paraoxon-contaminated water, the new bacte-
ria degraded the insecticides nine times more
efficiently than bacteria with OPH located in-
side their cells.

Several naturally occurring bacteria can de-
grade polychlorinated biphenyls (PCBs) to
chlorobenzoates, while others can degrade
chlorobenzoates to water, carbon dioxide and
sodium chloride (table salt). However, no single
bacterium is able to perform the complete de-
gradation of PCBs. UC Riverside plant patholo-
gist Dennis Focht genetically engineered a mi-
crobe to clean up chlorobenzoates.

Using a method he patented last year, Focht
is now creating these beneficial microbes natu-
really by introducing Pseudomonas aeruginosa,
which degrades chlorobenzoates. Focht found
that the indigenous Rhodococcus spp. bacteria,
which provide the primary process of break-
ing down the PCBs, transfer the desired genes
to the introduced bacteria, resulting in a more
stable strain than the genetically engineered.

"If nature can do it better, why not study how
to optimize the natural process?" says Focht.

Approaches to modi-
ifying tree growth. UC
Davis geneticists
Abhaya Dandekar and
Gale McGranahan have
modified walnut for im-
provement in root char-
acteristics of the root-
stock and bearing habit
of the scion. Dandekar
and McGranahan have
taken genes from
Agrobacterium rhizogenes, which stimulates root
production. They have introduced three genes
— rol A, B and C — from the bacterium to Para-
dox trees, a common walnut rootstock variety.
Field testing of the transgenic trees have shown
that they are vigorous and more compact than
nontransformed trees.

— Editor

Novartis commits $25 million to UC Berkeley

UC Berkeley and the Novartis Agricultural Discovery
Institute, Inc., have agreed to create a unique long-term agricultural
biotechnology research collaboration.

Under the terms of the agreement between Novartis and
the Department of Plant and Microbial Biology in the College of
Natural Resources, Novartis will commit $25 million over
5 years to support basic research in the department in the
area of agricultural genomics. It will also provide access to
proprietary technology and DNA databases, which will sig-
nificantly enhance the university's ability to do research at
the forefront of plant genomics.

In return, Novartis scientists will work closely with UC
Berkeley researchers, and the company will receive first
rights to negotiate for a fraction — roughly 30% to 40% — of
the discoveries made in the department. The fraction corre-
sponds approximately to the proportion of the department’s
total research budget provided by Novartis, and will vary
from year to year. Novartis, which was formed by the
merger of Sandoz and Ciba-Geigy, will pay patent costs, li-
cense fees, royalties and all other costs normally associated
with the commercialization of research, but the university
will own the patents and collect royalties on their use.

Gordon Rausser, dean of the College of Natural Resources
at UC Berkeley, says, "This is a valuable experiment, and
we’ll be monitoring it very closely to ensure that it produces
synergies that enrich public interest research."

Among the safeguards is a six-member Advisory Commit-
tee to oversee the contract, made up of three UC Berkeley
representatives and three Novartis representatives, as well as
a five-member Research Committee to award the grants. The
Research Committee will include three UC Berkeley faculty.